Scientific Abstract

GlobeImmune has generated recombinant yeast cell-based immunotherapeutics that target mutated Ras oncoproteins. Mutations in human *ras* genes and their encoded Ras oncoproteins have been implicated in the pathogenesis of multiple solid tumors, including pancreatic, colorectal, non-small cell lung cancer, ovarian cancer, and melanoma. The most common mutations in *ras* occur at codons 12, 13, and 61, all three of which result in constitutive activation of the Ras/epidermal growth factor receptor (EGFR) pathway and uncontrolled cell division. Because these mutations are not random, but are required for carcinogenesis, these mutated oncoproteins represent ideal targets for cancer immunotherapy.

G1obeImmune has developed a series of yeast *(Saccharomyces cerevisiae)* based mutated Ras immunotherapy products targeting these common mutations and has demonstrated in non-clinical models that these immunotherapeutics block the growth of tumors expressing mutations at the target positions in an antigen-specific fashion. Yeast are efficiently taken up by dendritic cells, resulting in an enhanced cell-mediated immune response aimed at cancer cells expressing mutant Ras protein. The GI-4000 series of Ras products is made up of three different immunotherapeutics, each of which carries the two most common mutated amino acid substitutions at the 61 position and one of the three most common mutations at the 12 position. These products have been tested in non-clinical safety studies in animals and been found to have minimal toxicity, generally limited to reactions at the injection site. The sponsor has filed an Investigational New Drug Application to initiate the evaluation of these products in patients with Ras-mutation bearing solid tumors.